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ARTICLE

Handling adverse drug reactions: state influence on access and availability of medicines in the former German Democratic Republic (GDR), 1949 to 1990

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Abstract

In the former German Democratic Republic, state institutions that controlled the supply of medicinal products were already established in the late 1940s and the early 1950s. These included Zentraler Gutachterausschuss für Arzneimittelverkehr (Central Review Committee for Drug Supply) and Institut für Arzneimittelwesen (Institute for Drugs). Both were involved in the assessment of adverse drug reactions. A reporting form was published in 1969. However, the number of reports was low, so developments in other countries such as the Federal Republic of Germany had to be considered. Using selected examples this article illustrates the actions that were taken to avoid damage caused by drugs, and shows that decisions were taken not only for medical reasons but also for economic and political ones. Ensuring adequate supply of drugs also had to be considered.

Zusammenfassung

Bereits Ende der 1940er- und Anfang der 1950er-Jahre wurden in der DDR staatliche Institutionen geschaffen, um den Arzneimittelverkehr zu überwachen. Hierzu gehörten der Zentrale Gutachterausschuss für Arzneimittelverkehr (ZGA) und das Institut für Arzneimittelwesen (IfAr). Der ZGA und das IfAr waren auch an der Erfassung und Bewertung von unerwünschten Arzneimittelwirkungen beteiligt. Ein Meldeformular wurde 1969 veröffentlicht. Aufgrund der geringen Meldezahl musste jedoch häufig die Entwicklung in anderen Ländern wie etwa der Bundesrepublik berücksichtigt werden. Anhand ausgewählter Beispiele untersucht der Aufsatz, welche Maßnahmen ergriffen wurden, um Arzneimittelrisiken abzuwehren. Dabei spielten jedoch nicht nur medizinische, sondern auch wirtschaftliche, politische und versorgungstechnische Aspekte eine Rolle.

Introduction

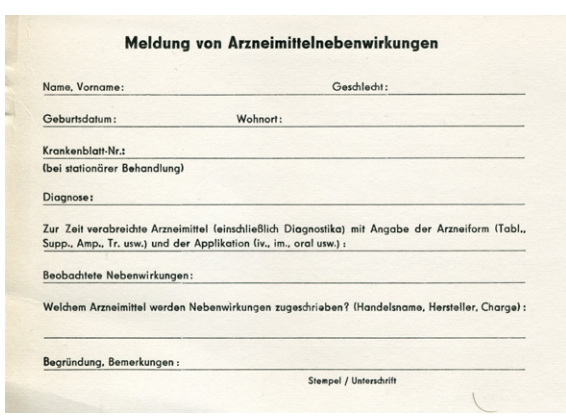
It was in 1949, precisely one day before the German Democratic Republic (East Germany) was founded on 7 October, that a regulation came into effect in the Soviet occupation zone controlling the distribution of medicinal products. From that date drugs had to be registered with the state.

A special committee called Zentraler Gutachterausschuss für Arzneimittelverkehr (ZGA) (the Central Review Committee for Drug Supply) advised the Ministry of Health on the registration or deletion of drugs.[1] From 1964 the ZGA also had to give its agreement before clinical trials could be conducted.[2] Members of the ZGA were clinicians, pharmacologists, pharmacists, medical practitioners, dentists and also representatives from industry. From 1960 sub-committees were created to discuss particular problems, for example those concerned with the supply of antidiabetic drugs. To coordinate the activities of the committee a secretariat was established; this has been situated in the state Institut für Arzneimittelwesen (IfAr) in Berlin since 1956.[3]

The IfAr, first established in 1950, also had to fulfil several other functions. For instance, the institute was responsible for the publication of the drug index and the revision of the pharmacopeia. The institute was also involved in the quality control of drug products manufactured by the pharmaceutical industry, and it also took charge of collecting reports of adverse drug reactions (ADRs).[4]

The adverse drug reactions reporting form 1969

For this purpose a special form was provided in the drug index since 1969 (Figure 1).[5] It contained information about age, sex, diseases and the administered drugs. At the end, doctors were requested to assess which drug might have caused the observed adverse reaction.[6] These measures were intended to make an important contribution towards increasing drug safety. For instance, it was stated that special recommendations with regard to drug therapy should be made based on incoming reports. In addition, a stimulus for drug development was expected.[7]



Meldung von Arzneimittelnebenwirkungen

Name, Vorname: Geschlecht:

Geburtsdatum: Wohnort:

Krankenblatt-Nr.:
(bei stationärer Behandlung)

Diagnose:

Zur Zeit verabreichte Arzneimittel (einschließlich Diagnostika) mit Angabe der Arzneiform (Tabl., Supp., Amp., Tr. usw.) und der Applikation (iv., im., oral usw.):

Beobachtete Nebenwirkungen:

Welchem Arzneimittel werden Nebenwirkungen zugeschrieben? (Handelsname, Hersteller, Charge):

Begründung, Bemerkungen:

Stempel / Unterschrift

Figure 1: *Reporting form published in 1969*

The reporting form published in 1969 was revised twice: from 1980 the severity of adverse reactions had to be assessed, and therapeutic measures had to be ex-

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plained. More details about the medication were required, such as the dosage and the duration of application. Allergies had to be mentioned as well.[8] From 1986 doctors had to assess whether a causal relationship existed between the administration of a drug and an adverse reaction. In this context, for example, the deviation of laboratory parameters was relevant.[9] Since that time, forms were no longer published in the drug index, but were provided by pharmacists.[10]

Between 1969 and 1970 the number of annual reports increased from 47 to 160, and there was a steady increase after that, but on average between 1969 and 1989 the IfAr did not receive more than 335 reports each year (Figure 2).[11]

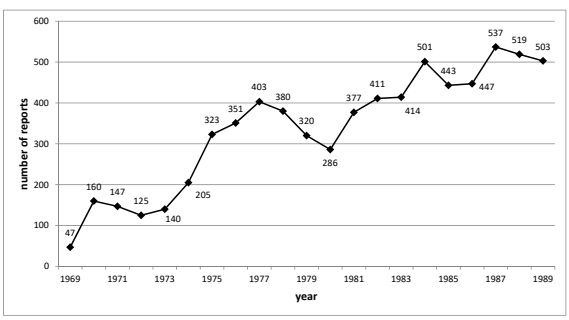

Figure 2: *Number of reports between 1969 and 1989*

Table 1 illustrates the number of reports compared to other countries. In Sweden 3,000 reports were received each year, which corresponded to 361 reports per million inhabitants. In the Federal Republic of Germany the number of reports amounted to 68 per million, and in the United Kingdom to 236 reports per million.[12]

Amongst the members of the Council for Mutual Economic Assistance, Czechoslovakia was the most successful country in generating adverse drug reaction reports. In that country adverse drug reactions had been reported since 1964. Czechoslovakia also participated as one of the first countries in the monitoring programme set up by the World Health Organization in 1968.[13] In addition, the country had coordinated the collection of reports of adverse reactions within the Council for Mutual Economic Assistance since 1979. The GDR had forwarded reports to the monitoring centre in Prague since 1982. However, the cooperation between the countries was assessed as ineffective.[14]

Initiatives designed to increase the reporting of ADRs in the 1970s and 1980s

In order to increase the number of reports in the GDR, several actions were taken, in particular in 1974 and in 1981. Since 1974 appeals had been placed in medical and pharmaceutical journals such as *Das deutsche Gesundheitswesen*[15] and *Medicamentum*[16], the last of which was edited by the pharmaceutical industry. The importance of reporting adverse reactions was also emphasized in central recommendations for therapy,[17] edited by the IfAr on behalf of the Ministry of Health. These recommendations served as guidelines for the diagnosis and therapy of diseases such as diabetes. They were written by experts in accordance with the medical associations.[18] In August 1975 the Minister of Health, Ludwig Mecklinger (1919-1994), also demanded that all incidents caused by drugs be reported to the IfAr.[19]

Table 1: *Number of reports compared to other countries*

Country	Reports per year	Reports per year per million inhabitants
Sweden	3,000	361
United Kingdom	13,000	236
Federal Republic of Germany	4,100	68
German Democratic Republic	335	21

In 1981 a directive came into effect regulating the storage and prescription of drugs. According to this directive adverse reactions had to be reported if they were unusual, required therapeutic measures, or a prolonged stay in hospital.[20] Adverse reactions were characterized as unusual if they were not listed in the current edition of the *Taschenbuch Arzneimittelsicherheit*,[21] a reference book in the field of drug safety containing information not only about adverse reactions but also about interactions, contra-indications and dosage. It was first released in 1983 and revised in 1986.[22]

Head lice products in the 1980s

Although doctors were requested to report ADRs in the 1970s, and although an obligation for them to do so was introduced in 1981 (and was later enshrined in the drug law of 1986)[23] the number of reports hardly increased until 1990. Only in one case, namely that of the anti-pediculotic preparation Arupex® which contained lindane (gamma-hexachlorocyclohexane), did accounts of adverse reactions lead to a modified benefit-risk assessment.[24] In the GDR products containing lindane, which were used against head lice, were available since 1969. The range included Delitex® Shampoo and Delitex® liquidum, the last of which contained 0.5 per cent of lindane in benzine, paraffin and propanol.[25]

Due to its flammability the adjuvants were replaced by isopropanol and propylene glycol and the lindane content was increased up to one per cent. In order to clarify the altered formulation, the product, now labeled as Arupex®, was newly registered in 1984.[26]

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Only one year after launch the IfAr received messages about adverse reactions. In August 1985 a mother applied Arupex® to herself and to both of her children. Contrary to the instructions for use the mother used a swimming cap instead of a towel to cover the head. Two hours later the mother and her eleven year old daughter complained of dizziness, vomiting and disorders of speech. The five year old son even suffered from respiratory depression.[27]

In November 1985 the IfAr was informed about another child suffering from headache and paleness after Arupex® had been applied correctly.[28] Because of these incidents a meeting of IfAr representatives and the chief physician of a paediatric clinic in Potsdam who had reported these adverse reactions took place in the same month. As a result it was recommended that the lindane content be reduced from 1.00 to 0.33 per cent, and that the instructions for use be revised.[29]

These new instructions now advised the user to cover the hair just with a towel, and in no case with a tight covering such as a swimming cap or plastic foil. Moreover, it was recommended that Arupex® be administered only once and no longer twice, that it be applied for not more than 60 minutes, and that the application be repeated only after nine days. Any preventive application was disapproved of. Finally it advised that babies should not be treated without the supervision of a physician.[30]

Against the background of the incidents depicted, the development of a drug containing permethrin as an alternative to Arupex® was demanded.[31] Though the ZGA had already recommended the development of such a medicinal product in 1982, the pharmaceutical industry was not able to realize it until 1988.[32]

Anti-diabetic agents in the 1970s

Unlike with Arupex®, in many cases the IfAr, the ZGA and the Ministry of Health had to rely on developments in other countries in order to draw conclusions for their own assessments of potential adverse drug reactions. In the late 1970s one of the issues the ZGA was concerned with was lactic acidosis, a severe metabolic disorder, which had been reported to be associated with the administration of biguanides, a group of antidiabetic drugs which included phenformin and buformin. Buformin, which had been launched in 1964, was the only biguanide available in the GDR. Additionally, the range of oral antidiabetic drugs available was limited to Maninil® and Orabet®. Both contained sulfonylureas; Maninil® contained glibenclamide and Orabet® contained tolbutamide.[33]

In the Federal Republic of Germany the issue of lactic acidosis caused by biguanides was first discussed in December 1976. As a consequence of these discussions the indications of the biguanides were restricted.[34] The East German Ministry of Health reacted to this development by calling upon the ZGA to investigate the availability of diabetic drugs in the country.[35] At its meeting in June 1977 the ZGA sub-committee recognized that national differences in the medical care of diabetic patients were considerable.[36] Since the 1950s a system had been established with the creation of specialist centres for diabetes where patients were attended to by experienced diabetic specialists. In all districts these care centres were set up as special departments in the so-called Polikliniken.[37]

According to the ministerial guidelines for the advanced struggle against diabetes from 1973, all therapeutic measures including drug prescription lay in the hands of these centres.[38] Likewise, the sub-committee noted the restricted indications that had already been implemented in therapy recommendations made in 1974. Accordingly, the administration of buformin had merely been recommended for overweight patients with type 2 diabetes.[39] These recommendations were revised in the following months. In particular, the daily maximum dose was reduced from 400 to 300mg of buformin hydrochloride. In addition, doctors were advised that the prescription of insulin and oral antidiabetics was reserved to the diabetic specialists exclusively.[40]

In March 1978 the withdrawal of phenformin and buformin was recommended in the Federal Republic of Germany.[41] After only a few days the East German ZGA sub-committee commented on this statement, and presented basically two alternatives. On the one hand, buformin could have remained included on the list of drugs available for the treatment of diabetes; but in this case the committee concluded that it would then be necessary to regulate its ever increasing consumption.

On the other hand, the deletion of buformin from the list was discussed. However, this option would have required a greater supply of Maninil®. For the production of this antidiabetic drug it would have been necessary to import raw materials from western countries, which would have caused considerable expenditure of foreign currencies.[42] In the end, the Ministry of Health decided against the deletion of buformin, because the greater provision of insulin also had to be considered.[43]

Hormone pregnancy tests 1978

In contrast to its decision regarding the antidiabetic drugs, the Ministry of Health banned the use of hormone pregnancy tests like Turignost® in the same year. The ban was made just a few weeks after the GDR me-

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dia had attacked the West German pharmaceutical company Schering AG,[44] which had launched the hormone pregnancy test Duogynon® in the 1950s. Duogynon®, marketed in the UK as Primodos®, came under suspicion of being teratogenic, and was therefore criticized in the West German media in the 1970s.[45]

The East German newspaper *Sächsische Zeitung* raised the issue too. Despite the fact that in the GDR similar tests had been used and that alternative immunological tests had not sufficiently been available, the story was headlined 'Nach Contergan vom Rhein jetzt Duogynon aus Westberlin: Schering gibt GIFT in den Mutterleib' ['After Contergan from the Rhine now Duogynon from West-Berlin: Schering administers poison to the womb'].[46] As a result of this publicity doctors and pharmacists became irritated and contacted the IfAr.[47] The ban was the result.

Analgesics in the 1980s

The analgesic, antispasmodic and antipyretic metamizole (dipyrone) became the subject of criticism in the Federal Republic of Germany in the 1980s because of serious adverse drug reactions such as agranulocytosis. As a result the ZGA chairman in the GDR warned the Minister of Health of the risk of a potential scandal similar to that in the case of Duogynon®/Turignost®, because in both countries metamizole was available without prescription.

After metamizole became available on prescription only in the Federal Republic of Germany in 1987, the ZGA did not make that recommendation for the GDR, because metamizole was frequently used for self-medication and alternative medicinal products often contained phenacetin which was frequently misused and assessed as harmful. Consequently, the ZGA demanded that the pharmaceutical industry replace phenacetin with paracetamol. Even though the committee had already made that recommendation in 1983 it took six years to implement it.[48]

Beta blockers 1975

Besides the assessment of approved drugs, the ZGA also evaluated drugs which had not yet been approved in the GDR. These included the beta-1-selective blocking agent practolol, originally developed by the British chemical company Imperial Chemical Industries. It was marketed as Eraldin® in 1970 in the United Kingdom and as Dalzic® in the Federal Republic of Germany. Since 1974 reports on adverse drug reactions had increased in the UK after several months or years of application. Cases of eye and skin changes such as psoriasis-like eruptions occurred, as well as otitis media, tinnitus, deafness and peritonitis.[49] Considering the adverse reactions, the distribution of Dalzic® was stopped in the Federal Republic of Germany in 1975. However, clinics were still expected to retain the product for use in 'special cases' in the future.[50]

At the same time in the GDR, practolol was still subject to clinical trials.[51] Due to the reported adverse drug reactions the application for approval was withdrawn and another clinical trial was not endorsed at the ZGA meeting at May 22, 1975. In addition, the committee urged the manufacturer VEB Arzneimittelwerk Dresden to examine the beta-1-selective blocker talinolol in a follow-up study.[52] In order to maintain the novel beta-1-receptor blocker, the structure of practolol was modified in Dresden.

Eventually, talinolol was selected from a variety of compounds.[53] The ZGA suggested that the beta-receptor blocker ought to be registered at least one year earlier than practolol in order to support drugs originally developed in the GDR.[54] The registration was recommended on 30 January 1975. As a result of the adverse drug reactions arising from practolol the committee had already demanded a follow-up study at that time.[55]

Conclusion

Efforts to control the range and availability of medicinal products in the German Democratic Republic were already in place in the Soviet occupation zone during the late 1940s. In this regard a special committee called Zentraler Gutachterausschuss für Arzneimittelverkehr (ZGA) became important. However, the poor economic situation, especially in the 1980s, was one reason for the pharmaceutical industry not being able to fulfil every requirement made by the ZGA and the Ministry of Health.

A second state institution, the Institut für Arzneimittelwesen (IfAr) later assumed responsibility for some aspects of the supply of medicinal products in the GDR. Amongst its responsibilities was the collection of reports of adverse drug reactions. Although several actions had been taken in the 1970s and 1980s, the number of reports remained low, so that the ZGA had to consider developments in other countries, in particular in the Federal Republic of Germany.

Nevertheless, the examples – including the antidiabetic drugs and analgesics available over the counter – discussed in this article demonstrate that the range of drugs available in the German Democratic Republic was taken into account as well.

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Further studies on some of the contents of an Italian seventeenth century pomade chest

Andrew Hardy

Abstract

Further studies have been done on the contents of two drawers (of three) in an Italian seventeenth century pomade chest/cabinet. Two samples from the top drawer, known to be soft soaps from previous work, were chemically analyzed to determine how they had been made. Unexpectedly, results show that they were made from a mixture of ruminant animal fat and a plant oil (probably olive oil). Empty containers from the bottom drawer had the words written on their waxed paper covers transcribed, translated and investigated. There is evidence that the chest was one of several gifts sent by the Grand Duke of Tuscany to Oliver Cromwell in 1657.

Introduction

In history it is not unusual for new information to be found that alters our interpretation of an event or of a person's actions. The 'story' can change over time as diaries, letters and other items are found (and if necessary translated) to give new insights. However, it is unusual for the 'story' to change in analytical science. Sometimes several interpretations are possible of the collected data, and sometimes they result from new data from a different analytical technique.

In this article I present new analytical chemistry data (and their interpretation) on the contents of two of the glass containers in the top drawer of an Italian seventeenth century pomade chest.[1, 2, 3] It is said to have been one of several gifts sent to Oliver Cromwell by the Grand Duke of Tuscany in 1657. This new data gives rise to some additions and amendments to previously published results.[2] Also presented here are some transcriptions and translations from the original hand-written old Italian found on the wax paper coverings of some of the empty glass containers in the bottom drawer of the chest. There follows a discussion of their most likely original contents and uses.

The chest, its provenance and the people associated with it

In May 1654, Ferdinando II de' Medici (Figure 1), the Grand Duke of Tuscany (1610-1670) who ruled between 1621 and 1670, instructed his English agent to acquire a portrait of Oliver Cromwell (1599-1658), who was Lord Protector of England between 1653 and 1658. By the end of the year a portrait had been purchased and delivered to him. Exactly which portrait he acquired is unclear; it could have been the famous 'warts and all' one painted by Sir Peter Lely (1617-1680) (Figure 2). Or it could possibly be the one reputedly done by Robert Walker (1599-1658).[4] However, this latter picture is sometimes attributed to Lely, and such a picture is now in the Uffizi Gallery in Florence. The more famous Lely picture is now to be seen in the Pitti Gallery of Florence.

Figure 1. *Ferdinando II de' Medici, Grand Duke of Tuscany*
(Source: Wikimedia Commons)

There is evidence that in 1657 the Grand Duke sent various gifts to Oliver Cromwell, one of which is reputed to be the stone inlaid Florentine cabinet (or chest), along with its contents (Figure 3) currently on display in the Oliver Cromwell Museum in Huntingdon, Cambridgeshire, UK. The cabinet's dimensions are as follows: 41cm wide by 36cm deep and 29.5 cm

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Figure 2. *Oliver Cromwell, Lord Protector of England (Source: Cromwell Museum©, Huntingdon, UK)*

high. The cabinet has been independently inspected by furniture historians and assessed to be a Florentine 'pietra dura' (literally 'hard stone') cabinet made in the period 1653-1658.[5] The contents of the cabinet's small glass tubs and pots (some of which can be seen in the foreground of Figure 3) are believed to have been made up by the L'officina Farmaceutica di Santa Maria Novella in Florence prior to the cabinet being sent to England.[6]

Samples and analytical methods and Results

The contents of the cabinet's original glass tubs and pots were all removed and placed in modern glass air-tight containers about forty years ago. Four samples from the top drawer were previously analyzed and found to be soft potassium soaps, and it was suggested that they had been made from olive oil.[2] Small amounts were also removed from two containers of the middle drawer and were analyzed. These initial results indicated that each sample contained in varying amounts; sodium palmitate, beeswax (and possibly some plant wax), and also cocoa butter and/or ruminant adipose fat.[3]

More data have recently been collected on these middle drawer samples, but have not yet been interpreted; this will be published in a later paper. Only empty containers are present in the bottom drawer, but most of these do have visible words, in Old Italian, written on their waxed paper coverings. Very few of the containers in the top two drawers have any writing visible on their plain non-waxed parchment paper coverings. A brief summary of relevant previously published analytical data will be presented in the Discussion section which follows.

For the top drawer samples two analytical techniques were applied. These were Fatty Acid Methyl Esterification (FAME) combined with Gas Chromatography-Mass Spectroscopy (GC-MS); and Gas Chromatography-Combustion-Isotope Ratios Mass Spectroscopy (GC-C-IRMS). These were applied to two of the top drawer samples, those labeled TD 2 and TD 4.[7, 8] The results are summarized below, with some additional data given in an endnote.[9]

Figure 3. *The Florentine cabinet and some containers (Source: Cromwell Museum©, Huntingdon, UK)*

Results of the FAME GC-MS and GC-C-IRMS analyses

For sample TD 2, ten of the 20 compounds identified were saturated straight-chain carboxylic acids (C7/8/9/14/15/16/17/18/19/20, to a total presence of almost 87%). Only two acids have percentage values greater than 5%; Palmitic acid (C16:0, 31.9%) and Stearic acid (C18:0, 41.0%). Additionally there were: two dicarboxylic acids (C8/9, to a total of 2.0% and where the C9:0 – Azelaic acid – is 1.3%); four isomers of C18:1 (to a total of 7.7%, where the isomer corresponding to Oleic acid is present at 2.6%); and four branched-chain saturated acids – one of C14:0 at 0.5%,

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one of C16:0 at 0.5% and two of C17:0 to a total of 2.0%.

For sample TD 4, nine of the 21 compounds identified were saturated straight-chain carboxylic acids (C7/8/9/14/15/16/17/18/20, to a total of almost 89%). Only two acids have percentage values greater than 5%; Palmitic acid at 33.5% and Stearic acid at 46.2%. Additionally there were: three dicarboxylic acids (C8/9/10, to a total of 2.6% and where the C9:0 has the highest value, of 1.7%); five isomers of C18:1 (to a total of 6.0%, where the isomer corresponding to Oleic acid is present at 1.7%); one isomer of C18:2 (at 0.4%); C14:1 (at 0.3%) and two branched-chain C17:0 (to a total of 1.4%).

Table 1: *Results of the GC-C-IRMS analyses*

TD 2 Sample	TD 4 Sample
δ^{13}C16:0 –28.58 ‰ (per mille)	δ^{13}C16:0 –28.31 ‰ (per mille)
δ^{13}C18:0 –30.41 ‰	δ^{13}C18:0 –30.25 ‰
$\Delta\ \delta^{13}$(C18:0 – C16:0) –1.83 ‰	$\Delta\ \delta^{13}$(C18:0 – C16:0) –1.94 ‰

The results of the GC-C-IRMS analyses are summarized in Table 1. The interpretation of these numbers will be presented in the Discussion section which follows below, which also includes translations of the Old Italian words found on some of the covering wax papers of the empty glass containers in the bottom drawer and a brief discussion of their original compositions and uses.

Discussion

Contents of the top drawer sample containers

In a previous publication four of these samples (TD 2/4/5/12) were studied and found to have only one crystalline (soap) salt present–potassium oleate.[2] This was done by comparing the low-angle/high d-spacing values from X-Ray Powder Diffraction (XRPD) data to fragmentary diffraction data in the published literature – to give a probable 'match' for this compound.[10]

However now, from the above FAME GC-MS data on TD 2 and TD 4, it can be seen that as there is very little oleic acid and large, and roughly equal, amounts of palmitic and stearic acids present, then the crystalline soap salt seen by XRPD cannot be the oleate salt. A potassium soap salt is present, as shown by the previous publication's Low Vacuum Scanning Electron Microscopy data (for elemental analysis showing a high percentage of potassium present) and Fourier Transform Infra-Red Spectroscopy (showing the presence of a hydrated soap) data. The samples are soft solids (as expected for potassium soaps) and one sample (TD 4) had, on its original parchment paper cover, the words, in old Italian, 'Saponetto di Fior' Aranci' – literally 'small soap with orange tree flowers' (Figure 4). In Renaissance Europe (between the fourteenth and seventeenth centuries) the word 'Saponetto', according to the *Treccani Dictionary* (the Italian equivalent of the *Oxford English Dictionary*), was a soap that was either solid or liquid, strongly scented and used for washing the hands and face and for perfuming small clothing items. Also, when some of this sample was mixed with a small amount of de-ionised water, an observable lather was obtained.[2]

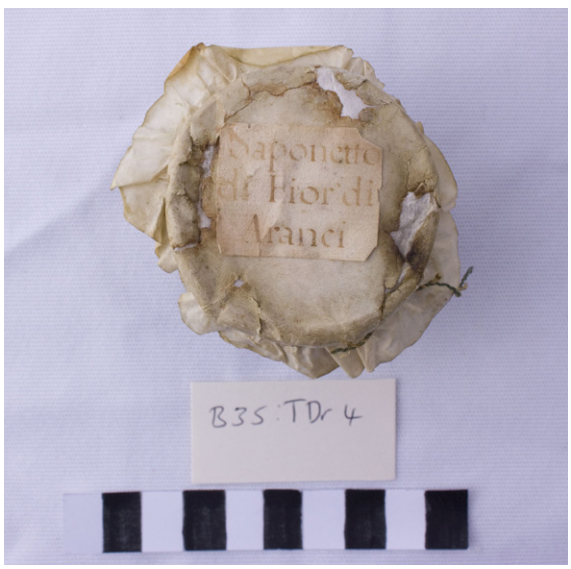

Figure 4. *Sample TD 4 and its labeled paper cover (Source: Cromwell Museum©, Huntingdon, UK)*

Using recently published XRPD data on a range of crystalline potassium soap salts,[11] and also using the predicted values for the observed (largest) d-spacings for soap mixtures given in a separate study,[12] then for the (essentially) binary soap crystalline mixtures (where the percentage presence values of the palmitic and stearic acids are close to each other and much larger than for other acids present) in my samples, I have as predicted, d-spacing values that are intermediate between those of the potassium palmitate and stearate salts.

Were these soaps made using olive oil?

It was previously suggested that these soaps were made using olive oil.[2] To determine if this is in fact correct the previously summarized FAME GC-MS and GC-C-IRMS data will now be interpreted. The FAME GC-

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MS data on samples TD 2 and 4 showed only the presence of a degraded fat or oil (though a mixture is also a possibility). There is a small number of oxidation products – that is a few short-chain dicarboxylic acids and no oxo-/hydroxy-/dihydroxy- derivatives. The presence of both mono- and di- carboxylic C9:0 acids suggest an original larger amount of oleic acid (C18:1).[8]

The presence of palmitic (P, C16:0) and stearic (S, C18:0) acids in significant and similar amounts combined with the presence of small amounts of: odd-numbered saturated acids (C15:0, C17:0 and C19:0), multiple isomers of C18:1 and various branched-chain saturated acids (C14:0, C16:0 and C17:0) – are all indicative of the presence of animal fat.[8, 13, 14]

The calculation of various fatty acid ratios can be done, and using various discriminatory values the type of fat/oil can be indicated. Such indications should be used with caution as exceptions (to the discriminatory values generally used) can occur, and complications can arise if a mixture is present. If possible these ratios should be combined with additional information.[14]

The most well-known of these ratios is the palmitic acid/stearic acid ratio (P/S, C16:0/C18:0). A cut-off value of 1.3 is often used; where P/S > 1.3 this suggests the presence of non-ruminant (usually taken to be porcine) fat; and if P/S < 1.3 then ruminant (i.e. bovine or ovine) adipose fat is indicated. The ratios in this case are 0.78 for TD 2 and 0.72 for TD 4, indicating a ruminant adipose fat for both samples.[13, 14]

A second fatty acid ratio is a combination of two ratios: stearic acid/palmitic acid (S/P) along with C17:0 br. (branched-chain)/C18:0. If S/P is > 0.5 then terrestrial animal fat is suggested; if S/P < 0.5 then plant oil or marine animal fat is indicated. If C17:0 br./C18:0 is < 0.02 then non-ruminant fat is suggested, and if it is > 0.02 then ruminant fat is indicated. In this case the values for TD 2 and TD 4 respectively are: S/P = 1.28 and 1.38, and C17:0 br./C18:0 = 0.048 and 0.030. Ruminant fat is therefore indicated for both samples.[15]

The last fatty acid ratio is (C15:0 + C17:0) / (C12:0 + C14:0 + C16:0 + C18:0). When this ratio > 0.04 then ruminant fat is suggested; if it is < 0.04 then non-ruminant fat is indicated. The TD 2 and TD 4 values are 0.060 and 0.041 respectively, once more indicating the presence of ruminant fat.[16] Thus, overall from these three fatty acid ratios ruminant fat is indicated, and furthermore, from the P/S ratio, it can said that ruminant adipose fat is indicated.

Supporting evidence from additional analytical data

Results from fatty acid ratios should be combined with other data if at all possible; these can include historical records (such as recipes) and additional analytical data. The analytical technique often used is GC-C-IRMS. Measurements from this technique, on an unknown fat/oil-containing residue, are compared to values from modern-day reference fats/oils and so the unknown fat/oil can be identified.

By measuring the carbon stable isotope (i.e. ^{13}C vs. ^{12}C) ratios, usually expressed as $\delta^{13}C$ values for the FAs (fatty acids) C16:0 and C18:0, it was found to be possible to distinguish fats/oils of different origins. Reference data, enclosed within confidence ellipses for each type of modern-day fat/oil studied, are placed on a plot of $\delta^{13}C18:0$ vs. $\delta^{13}C16:0$. The number of ellipses have increased over time and there is now sometimes a degree of overlap between some of the ellipses.[8]

I have compared my data range[9] to several such reference plots and found that it is mostly in-between two ellipses – those for ruminant adipose fat and C3 plant oils, where C3 is one of the three metabolic pathways for carbon fixation in photosynthesis of plants. There is a degree of overlap of my data with the reference ruminant adipose fat ellipse (of about 30%), and whilst no actual reference data for a specific C3 plant oil directly overlaps with my data, the closest plant oil data is that for olive oil.[17, 18] Thus, the above plot shows we have a mixture, which was used to make our soft soaps, of ruminant adipose fat and a plant oil (probably olive oil). The ruminant fat is the larger component of the mixture, with the (olive) oil being present in a smaller amount. To quantify the amounts of these components present will require future theoretical calculations and/or experimental measurements on suitable mixtures of known composition.

Additionally, $\Delta\delta^{13}$ (C18:0 – C16:0) can be plotted against $\delta^{13}C16:0$. Three horizontal bands were generated using reference data and these are (with approx. numerical ranges given in brackets): the most negative $\Delta\delta^{13}$ values are for ruminant dairy fat (-6 to -3); less negative for ruminant adipose fat (-3 to -1) and mostly positive for pig adipose fat (-1 to +2).[8, 17] My average $\Delta\delta^{13}$ value is -1.89 ‰ and is in the ruminant adipose fat band. One of the few publications which have placed their C3 plant oil GC-C-IRMS data on this type of plot found that for the six oils studied the $\Delta\delta^{13}$ range was approximately -2 to +1, with most of the values being in the pig adipose fat range.[17]

Supporting evidence from historical records

A very old written recipe for soft soap – albeit in a very crude and impure form – has been found at Girsu (modern-day Tello, Iraq). It has been dated to the third dynasty of Ur (c.2100 BC). The recipe is the combination of oil (approximately one litre) and potash (approximately 5.5 litres); where the potash is assumed to be

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the impure potassium carbonate in wood ash. It was used to de-grease and clean cloth.[19]

Almost two millennia later Pliny the Elder (23-79 AD) gave another recipe for soft soap. He stated that it was first invented by the Gauls and Germanic tribes of Northern Europe and primarily used to dye and bleach their hair.[2, 19, 20] The translation gives the recipe:

> 'Soap is the invention of the Gauls and this is used to redden the hair. It is made from fat and ashes – the best is beechwood ash and goat fat, the two combined thick and clear. Many among the Germans use it, the men more than the women'.[20]

It is unclear, for the above recipe, if the ashes mentioned were converted to impure caustic potash (i.e. potassium hydroxide) and then reacted with the goat fat to give a soft soap very similar to one made in the seventeenth century. However, in the Roman Empire of the second century AD, it is thought that such conversion was being done to make soft soaps used for both clothes and body washing.[2, 19, 20, 21]

The making of soap, often on a small scale by the formation of a craft guild, slowly spread throughout Europe. One of the first recorded such guilds was in Naples of the late sixth century AD. By c.700-800 AD soap-making was an established craft industry in Italy and Spain. The original Castile soft soap was said to be made at this time in Spain using olive oil, wood ashes and perfume. By the thirteenth century soap-making was established in Bristol, Coventry and London in England. Initially the manufactured soft soap was imported, but by the 1500s the olive oil was imported to make such soap in England. It was used alone or combined with tallow for making soft soaps at first, and later (from c.1700) increasingly for making hard bar soaps, which took longer to make, but were easier to handle and did not require tree ashes.[2, 22, 23]

Soft soap recipes in Italy before 1700

Information on soft soap recipes, using olive oil as an ingredient, in Italy before 1700 is sparse. In Savona of the 1500s olive oil was mixed with laurel berry or seed oil to make soap, but it is unclear if this is soft or hard bar soap. Given the time period it would be expected to be soft soap. Also, no specific information could be found for a soft soap recipe using olive oil and tallow. However, it would be expected that any given country making soap at this time would probably largely use what was readily available within the country, and Italy usually had a plentiful supply of olive oil and tallow (i.e. bovine/ovine adipose fat). Thus a recipe such as ours, where the olive oil has been diluted with tallow, could have been a common occurrence rather than the result of lack of olive oil because of a bad olive harvest. Such a recipe could have been the result of experimentation to give a soft soap of desirable qualities, such as increased stability to reduce it becoming rancid and having an acceptably (small) degree of skin irritation when used on human skin.[24]

Over time soaps have been variously used medicinally. For example, they have been used externally as a treatment for skin diseases, burns and sores. They have been taken internally for relief from 'gravel' (urinary stones), as a mild antacid or laxative, and Castile soap pills were taken for the relief of dysentery. Soap has been used as a non-toxic filler of pills in general, and as a pseudo-active ingredient in a whole range of quack medicines.[2, 23, 25, 26]

Some examples of specific medicinal uses of soft soaps are: 'liquid' soap (taken to be soft soap) is listed as an ingredient in several recipes for the treatment for burns in the early seventeenth century;[27] as a recipe for an enema (an unspecified soft soap diluted twenty times with warm water) in Theobald's 1752 *New Compendious Dispensatory*;[28] and today a dilute aqueous solution of potassium oleate has been found to be a very effective pesticide against cockroaches.[29]

Figure 5. *Sample BD 4 and its labeled waxed paper cover*
(Source: Cromwell Museum©, Huntingdon, UK)

Contents of the bottom drawer sample containers

Ten of the thirteen empty glass containers (labeled BD 1 to BD 13 by the Museum) in the bottom drawer of the chest have Old Italian writing on their wax paper coverings (see Figure 5 for one example, BD 4). My current best transcriptions and translations into English of these hand-written words are as follows:

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BD 2, BD 5 and BD 9 reveal the words 'Manteca (abbreviated to 'Mj' or 'Mj^{ca}') di Gelsomini', which translates as 'Ointment (or butter) of Jasmine". BD 1, BD 7 and BD 12 disclose the words 'Manteca (abbreviated as before, or even omitted altogether for BD 1) di Melangoli', which translates as 'Ointment of Bitter Oranges'. BD 3, BD 4, BD 10 and BD 13 shows 'Manteca (where this word, written in full, is only present for BD 4) di Caceia', which I believe best translates as 'Ointment of game' (i.e. the fat of a hunted game animal, such as wild deer, pig or boar).

The BD pots were empty of contents when the chest was loaned to the Cromwell Museum over four decades ago. There are two possible reasons why they were empty: firstly, all the contents in all the pots were rapidly used by descendants of Oliver Cromwell; or secondly, and perhaps more likely, the game fat used in their manufacture rapidly became rancid, and so gave rise to offensive smells that resulted in the pots being emptied.

Jasmine extract, or its essential oil,[1] is used as a topical medicine (usually as a small amount in a base material), for the relief of dry, sensitive or irritated skin. It is also used for muscle sprains and spasms, and as a skin massage agent it induces relaxation.[30] Bitter orange extract/oil has various medicinal uses, where it can be ingested (heavily diluted) or applied topically (as for jasmine above). Used topically it is relaxing and sedative, and so is used to encourage sleep. However, it can sometimes cause skin irritation and should be used heavily diluted and used with care.[31]

Wild animal (i.e. game) fat was known and probably used topically in Tuscany of the seventeenth century – perhaps mixed with a coloring agent and a herbal or inorganic active ingredient. Domesticated pig's fat was used in skin ointments – for example it was found in two of four recently analyzed skin ointment residues, dated to the sixteenth and seventeenth centuries, from labeled containers in the Aboca Museum (Arezzo, Italy).[32] Additional, non-medicinal, uses of scented ointments/pomades will be mentioned later.

Scented ointments/pomades of the seventeenth century were often made by cold (enfleurage) or hot (maceration) absorption of fragrant molecules into a base material of fat/oil.[1] A base material of the period, such as 'Leaf of Hogs-fat' (i.e. lard), would have been repeatedly washed to remove as much of its odor as possible before fresh flowers of jasmine would be used to cover the base when it was laid out in trays, for the enfleurage process.[33] Bitter orange extract can be simply obtained by the method of 'expression' (that is by squeezing, here of the inside fleshy part of the peel of the fruit) and then adding as required to a de-odorized fat/oil.

Recipes for scented ointments/pomades

Many recipes for scented ointments or pomades existed in the past, and some examples are: a pomatum 'to refresh the complexion' made of lard, sweet almond oil and apples' parts; 'pomatum for the lips' made using butter, Virgin wax (i.e. fresh beeswax), black grapes and orange-flower water; various 'floral waters' which contain very small amounts of dissolved odorant material from rose, lavender or orange extracts and which were used for food flavoring or even as a beverage; and a pomade recipe is mentioned by Dioscorides (c. 40-90 AD) in his *De Materia Medica*, which he called Iasmelaion and was made from sesame oil and the white flowers of jasmine – being recommended for use on the whole body after bathing 'for those that want warmth and relaxation'.[33, 34, 35]

The various aroma molecules are often very volatile and so quickly evaporate/degrade under the action of heat, light, moisture and oxygen. Thus all that usually remains in an old residue of a scented ointment/pomade is the degraded base material.[35] A rare example of a possible remnant of a plant part being found was in the analyses of the amorphous residues found in seven Roman glass unguentaria. They were dated to between first century BC and first century AD, and were excavated from a Roman villa in the ancient town of Oplontis (about 20 km south east of Naples, Italy). Apart from beeswax and pine resin found in all the containers, the presence of a plant-waxy-lipid was also suggested. The authors suggested that this last material was from the wax of the plant part(s) (possibly a leaf or flower) used in maceration or enfleurage to make the original scented skin ointments.[36]

Additional non-medicinal uses of scented ointments/pomades over time have included: anointing the living and embalming the dead; to create a pleasant aroma at feasts/social gatherings; for individual use after bathing either at home or after exercise at the gymnasium; to scent clothes/gloves/leather-work; to keep 'evil spirits'/insects/plague at bay and to cover up skin defects of old age or caused by disease.[34, 35]

Conclusions

The new data from two analytical techniques (FAME GC-MS and GC-C-IRMS) have shown that, for the top drawer samples, a new interpretation of their origins is required. These samples are still potassium (soft) soaps, but are now shown to have been made from a mixture of ruminant adipose fat (i.e. bovine or ovine fat) and a smaller amount of a plant oil (probably olive oil). This recipe could be one commonly used for soft soap-making in Tuscany of the seventeenth century, *or* it could be one specially devised for these samples to

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give soaps that would not readily turn rancid and that could be used on the hands and face with minimal skin irritation. The latter may or may not now be true, but the samples are not now obviously rancid. One of our samples studied (TD 4) was definitely scented and some/all of the other top drawer samples may well have also been (differently) scented originally.

The bottom drawer samples were probably intended as scented pomades/pomatums for the hair or as scented ointments/unguents/balms for the skin. As to how medically efficacious they would have been when applied to the hair/skin is unclear, but they would at least have covered/protected a skin ailment and would have smelt pleasant initially. However, this probably did not last as the game fat used as their base material would have become rancid eventually, resulting in all the pots being emptied of their contents.

The changes in origin of the top drawer samples shows that any given explanation must often in reality be limited and considered to be, at least to a degree, as preliminary. This is here caused by: degradation effects over centuries, the complexities of interpreting sometimes apparently contradictory analytical data and by the paucity of direct documentary evidence of the recipes used to make the original samples. The process towards a better understanding of these samples can therefore also be described as an iterative one. This process is greatly helped by a multi-analytical approach and from having access to relevant historical information.

Oliver Cromwell and the Grand Duke of Tuscany

The only information we currently have of Cromwell's reaction to being given various gifts, including 'oils and essences' (assumed to refer to the contents of this pomade chest), from the Grand Duke of Tuscany is from a report written by Francesco Giavarina (the Venetian Resident in England) to Venice on 25 May 1657. The translation of the relevant part of his report is given below:[37]

> 'Salvetti, the Florentine Resident, has recently presented the Protector in the name of the Grand Duke with a dozen butts of different wines, expressly sent from Tuscany, with a quantity of other fancy food stuffs, oils and essences which his Highness has made and distilled. Cromwell is gratified although the wine has much deteriorated on the voyage. But the Protector has no great taste for anything and he is not disposed to regard favourably presents of this character. One of his physicians has stated that he has not the courage to put such liquors to his lips. He is possibly afraid that they will be bitter, being fearful of his own shadow, so to speak, and living in constant apprehension of everything, for he trusts no one'.

Whilst some of this may well be an exaggeration, it is most likely broadly accurate.

Acknowledgements

I would like to thank Dr. John Goldsmith, former curator of the Oliver Cromwell museum in Huntingdon (Cambridgeshire, UK) for initiating this project and for four images (Figures 2, 3, 4 and 5); Dr. Anita Santorum for translations of old and modern Italian, plus for relevant information obtained from various Italian sources; Ms Sally Pointer (an Independent Experimental Archaeologist) for numerous discussions on matters archaeological and cosmetological; Dr. Val Steele (University of Bradford, UK) for discussions on the interpretation of the GC-C-IRMS data; and Hall Analytical Laboratories (Manchester, UK) for the two TD samples' FAME GC-MS and GC-C-IRMS analyses.

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Endnotes and References

1. A 'pomade' (sometimes pommade or pomatum) is here taken to be a scented greasy substance, which can be liquid/sticky semi-solid/soft solid, and is often described as being used for the hair or skin of the scalp. However, this term can also be used more generally, and may refer to any scented ointment/unguent/balm intended for use anywhere on the skin. They consisted of one or more fats/oils, of minimal smell, sometimes with added wax or resin, mixed with one or more scented extracts/oils (sometimes referred to as essential oils). In the past the 'pomade' was usually made by enfleurage or maceration – that is, the cold or hot respectively absorption into a base material such as a fat or an oil of the odoriferous (and usually volatile) molecules of various fragrant plant/fruit/animal parts. The essential oil could then be extracted, if required, from the scented ointment/pomade by dissolving it in alcohol, followed by steam distillation. An essential oil is here defined as a concentrated hydrophobic liquid containing volatile aroma compounds from parts of plants/fruits/animals. More details, and associated references, are given in the Discussion section.

2. Hardy, A. and Rollinson, G. A chemical study of some seventeenth century Italian soaps. *Pharm Hist (Lond)* 2011; 41(4): 58-64; and references therein.

3. Hardy, A. and Rollinson, G. Two seventeenth century skin balms for warts and pimples? *Pharm Hist (Lond)* 2016; 46(3): 50-55; and references therein.

4. Crino, A.M. and Millar, O. Sir Peter Lely and the Grand Duke of Tuscany. *Burl Mag* 1958; 100(661): 124-131.

5. The cabinet and its contents are on loan to the museum from a descendant of Oliver Cromwell's fourth son, Henry Cromwell. The cabinet has been variously described as a pomade,

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balsamari and 'cassette per profumi' (box for perfumes/scents) chest. The glass pots or tubs in the first and second drawers are covered with semi-porous parchment paper; this in turn has been covered with fabric where some of the parchment paper has degraded or darkened over time. The pots in the third, bottom drawer are covered with waxed paper, where some have words written on them in old Italian, and the waxed paper is itself covered with fabric. Their waxed paper covers are less degraded. The glass used for the top drawer pots is brown, largely opaque and referred to as Calcedonio glass. White glass is used for the pots in the other two drawers.

6. Unfortunately, though the pharmacy agrees that it did make gifts for this Grand Duke, they have been unable to find evidence that they made these particular samples. The website address for this famous pharmacy in Florence is: www.italian.it/santamarianovella/smnuk.htm.

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The main components of fats and oils are triacylglycerides (TAGs), where each of these molecules is an ester of glycerol and three carboxylic acids. These acids are of variable carbon chain length and can be saturated or unsaturated. In old fats and oils the TAG molecules are often partially hydrolyzed to their component fatty acids (FAs). Also, these FAs and TAGs can be subject to oxidation – especially at the carbon to carbon double bonds in the carbon chain. Degradation can additionally occur by the action of any bacteria or microbes that may be present. Thus oleic acid (C18:1) is expected to degrade, especially with respect to oxidative cleavage at its carbon-carbon double bond, much more over time than the saturated palmitic and stearic acids.

FAME GC-MS and GC-C-IRMS: These analyses were each done using well established experimental protocols. For more information on these two techniques see references 7 and 8; additional information on our experimental details can be obtained by contacting the author. The estimated errors in the δ^{13}C16:0 and δ^{13}C18:0 values respectively, for the two TD samples are: ± 0.32 and 0.03‰ for TD 2 and ± 0.28 and 0.49‰ for TD 4. The range of both samples' values, using the values given in the results section and the errors given here, is the data range used to compare with reference data mentioned in the Discussion section.

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'To be taken very slowly': The story of Fudge's firewater

Philip Strange

Abstract

Fudge's Firewater was the nickname given to a cough medicine that was made and sold from the mid-1950s at the pharmacy of Kenneth Fudge in the small market town of Bridport in Dorset in south west England. Its proper name was Fudge's Mentholated Honey Syrup, a local variant of Gee's Linctus. Its main ingredients were camphorated tincture of opium, oxymel of squill and tolu syrup, to which menthol had been added. Despite ownership of the formula and the place of sale changing several times over the next 50 years, the product is a rare example of a nostrum that survived into the twenty-first century.

Introduction

Until 2006, in the market town of Bridport in the south west of England, the local population had access to a remarkable cough medicine that really seemed to work. The medicine was Fudge's Mentholated Honey Syrup, or, as the locals christened it, 'Fudge's Firewater'. The story begins in the 1950s when a Mr Ken Fudge in Dorset started to make and sell his own nostrums, at a time when every pharmacy had their own range of cough syrups, indigestion mixtures and throat pastilles. Most nostrums ceased to be available after implementation of the 1968 Medicines Act, but 'Fudge's Firewater' survived into the twenty-first century.

Many local people had fond memories of the product, and Fudge's Firewater soon entered local folklore. Its content, preparation and uses can thus readily be ascertained from surviving sources, and people's experiences of it have been captured by means of a 'Memories of Fudges Firewater' call on Facebook.[1] This short article tells the story of this potent mixture, what it contained, how it was used and why it is no longer available, using material from a variety of sources.[2]

Mr Fudge and his pharmacy

Kenneth Charles Fudge was born and brought up in Blandford, a market town in north Dorset, a county in the south west of England. He trained as a pharmacist and qualified in 1933, having undertaken his apprenticeship in Blandford. He appears to have spent the early part of his career in London, since in 1955 he was living in Edgware. However, around that time he returned to his native Dorset, moving from London to Bridport, another market town, not far from the south coast. He opened a pharmacy in West Allington, next door to the shop of Balsons, who were Britain's oldest family butchers, having been established in 1515.

Figure 1. *Mr Fudge's Pharmacy in the late 1950s, when the road was flooded. Mr Fudge is seen standing in the shop doorway with Donald Balson from the next door butchers' shop in front (Source: Photo kindly supplied by Richard Balson)*

Fudge's was a traditional pharmacy that sold the usual range of toiletries, cosmetics and photographic requisites, in addition to having a thriving trade in the sale of over the counter medicines and a busy prescription dispensing service. A Kodak sign was displayed prominently above the door, and attention to the pharmacy was drawn by a magnificent sign on which the word 'chemist' appeared below a mortar and pestle and which hung above the shop window. The only downside was that the street outside was subject to occasional flooding.

The origins of Fudge's Firewater

In the mid-1950s, many pharmacists devised their own remedies, often to secret recipes, and Mr Fudge was no exception. He made several nostrums, the name given to those remedies produced and sold in a single pharmacy, but the most popular and enduring was his Men-

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tholated Honey Syrup (known locally as Fudge's Firewater).

Table 1: *Key dates in the story of Fudge's Firewater*

Year	Event
1950s	Mr Kenneth Fudge opens his pharmacy at 7 West Allington, Bridport and begins production of Mentholated Honey Syrup ('Fudge's Firewater').
1973	Mr Fudge retires, and the recipe for Firewater transfers to Mr Joe Sparrow at his 24 East Street Pharmacy.
1975	Mr Kevin Morrish takes over the East Street Pharmacy, together with Fudge's Firewater.
1998	Mr Morrish retires and sells the business which is then acquired by the Lifestyle Pharmacy Group.
2001	Moss Chemists Ltd acquires the East Street Pharmacy. Mr David Conroy is the manager until 2005.
2006	The owners Moss Pharmacy, subsequently rebranded as Alliance Pharmacy, cease production of Fudge's Firewater at its Bridport branch.
2006-2009	Fudge's Firewater continues to be available in Weymouth, at the St John's Pharmacy of Mr Dipan Shah, but only with a private prescription.
2009	Fudge's Firewater ceases to be available.

Mr Fudge's medicine was a dark brown syrupy liquid made by mixing menthol crystals and a little fudge flavouring into Gee's Linctus, itself an old-fashioned cough remedy dating from the Victorian era. Gee's Linctus, otherwise known as Compound Squill Linctus, or Opiate Squill Linctus of the British Pharmaceutical Codex (BPC), contains several potentially active ingredients.

Gee's Linctus consisted of equal volumes of camphorated opium tincture, oxymel of squill, and tolu syrup. The tincture of opium was an alcoholic extract of opium, the resin derived from opium poppies. The main active ingredient in opium is morphine, a substance with an established effect on cough[3], but also a well-known drug of abuse. Because the linctus contained morphine but only at low levels (<0.02%), it was categorised as a schedule 5 controlled drug (Misuse of Drugs Regulations 2001)) and could be supplied through a registered pharmacy without a prescription. Squill, a plant extract, was another potentially active component in the linctus that, paradoxically, encourages coughing and mucus removal. The medicine also contained alcohol at similar levels to a fortified wine, and this may have contributed to the Firewater experience.

Mr Fudge's masterstroke was to boost the effects of the Gee's Linctus by adding menthol, a remedy used for many years to help with symptoms of coughs and colds[4]. The menthol may also have acted as an oral anaesthetic, helping with sore throats, and it may have relieved nasal congestion.

Although cough medicines cannot alter the course of viral infections they may help the patient feel better. Fudge's medicine attacked symptoms in several ways. It was the menthol, however, that made the potion so memorable, justifying the Firewater nickname and establishing a shared experience among those who used it, believed in it and benefited from it.

As a result of its capacity to help patients feel better it became extremely popular and a very successful nostrum. It is clear that it was made in very substantial quantities. People travelled long distances to purchase the medicine. Holidaymakers reportedly often went home with extensive supplies, and during some winters as many as 250 bottles of Fudge's Firewater were sold each week at the East Street Pharmacy.[5]

Following the introduction of the 1968 Medicines Act, many nostrums and proprietary medicines disappeared because of the new regulations on licensing. Fudge's Firewater persisted into the 21st century because it was exempt from licensing (see section 10 of the regulations) being a nostrum made in a registered pharmacy for sale in that pharmacy with no advertising.

The recommended uses of Fudge's Firewater

Fudge's Firewater was an old-style cough medicine recommended for common winter ailments: coughs, colds, influenza, loss of voice, hoarseness, sore throat and catarrh. The dose was one teaspoonful [5 ml] every four hours, but the label warned ominously that each spoonful should be 'taken very slowly'. It was sold from the pharmacy over-the-counter without prescription, but strictly under the control of the pharmacist.

Fudge's Firewater was immensely popular, and many people have told the author how much they trusted it to help their symptoms. Typical comments were 'a brilliant cough mixture, couldn't beat it', 'an amazing medicine for coughs and sore throats', 'never bought anything else', and 'please, if there is a God, bring back Fudge's Firewater'.

The medicine had a formidable reputation amongst its users. Comments included 'it nearly blew your head off, but by golly it did the trick' and Gail Reichter recalled that 'the menthol did take your breath away'.[6]

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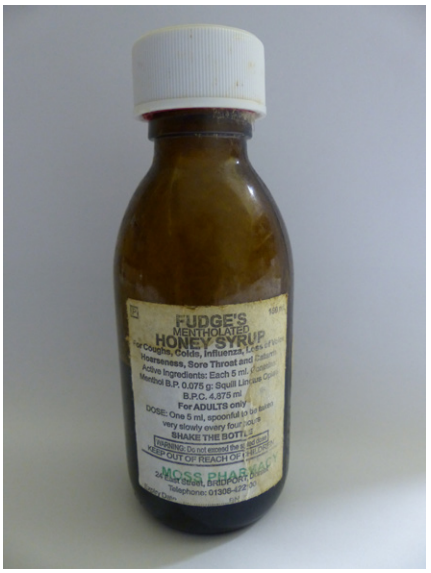

Figure 2. *A bottle of Fudge's Mentholated Honey Syrup (Fudge's Firewater) (Source: Photo kindly supplied Emily Hicks, Bridport Museum)*

Some of these effects may have been caused by the menthol accumulating at the surface of the medicine when it had not been fully mixed. Some experienced rather more serious symptoms. Margery Hookings recalled that

> 'It tasted like red diesel mixed with the finest brandy-lovely. And as it shifted your fever you hallucinated at the same time. I remember being tucked up in bed with flu in my damp, rented cottage in the middle of nowhere and peeping out of the covers to see a demon-like face made up of lots of dots, zigzagging all over the woodchip wallpaper. One minute it was smiling, the next scowling, possibly at the interior design. Scary but interesting.'[7]

It was not the easiest medicine to take, and some patients commented on this. 'It was a trial to take, but you knew it would make you better' and several people spoke of 'the Fudge's shudder'. As Mr Fudge himself said: 'Some do swear by it, some do swear at it'.

Even now, more than a decade after the medicine was discontinued in its home town, the mere mention of the Fudge's name evokes a warm wave of nostalgia and longing in many Bridport people.

Unconventional uses of Fudge's Firewater

Its growing reputation led to its use for a number of less conventional purposes. The medicine was a voice-saver for some professional singers, and the author has heard about one well-known entertainer who would regularly send a friend to buy Firewater from Mr Morrish to help lubricate her vocal cords. Another fan of the product was Marco Rossi. He recalled that

> 'In the mid-to-late 1990s I was the guitarist/vocalist in a band called Stocky Lamaar, who essentially ran on Fudge's. At the time, bassist/vocalist Al and myself played a whole heap of gigs in smog bound, pre-smoking ban pubs around Dorset with a variety of different but uniformly noisy line-ups, which inevitably meant that we were yelling ourselves hoarse on an almost nightly basis. We tried everything to remedy this (apart from giving up smoking!) and I even went to a throat specialist at one point.
>
> At this juncture, like a living advert tagline, our pal Pete said 'have you tried this?' and produced a bottle of Fudge's…and that proved to be the miracle cure. Nothing I've tried before or since has ever cut to the chase with such brute fervour. It felt as though it just punched straight through the throat strata of detritus and fag ash, leaving you suddenly able to breath properly, and sing without sounding like Madge from Neighbours at a Bonnie Tyler tribute karaoke night. After that a bottle of Fudge's became as essential a component of my guitar case as spare strings and leads. Anyone who remembers Stocky Lamaar from the time will remember that Al and I would have a bottle apiece resting on each of the PA speakers.'[8]

Abuse of Fudge's Firewater

Non-prescription medicines such as Gee's linctus, and variations of it such as Fudge's Firewater, have been abused by people trying to access even the small amounts of morphine they contain[9]. Gee's linctus, for example, is reported to induce a 'lovely euphoria and dreaminess'[9], but only if the user is prepared to drink 50ml or more of the medicine at a time. Local pharmacists were aware of the problem and tried to control it: Mr Morrish monitored all sales of Fudge's Firewater personally, and Mr Conroy, the manager in the early twenty-first century, restricted sales to one bottle per person, with a signature.

The end of Fudge's Firewater

Fudge himself retired from his pharmacy in 1973, and the recipe for Firewater transferred to Mr Joe Sparrow at his pharmacy at 24 East Street, Bridport. That pharmacy was itself taken over in 1975 by Mr Kevin Morrish, and Fudge's Firewater continued to be made and

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sold under his supervision. Mr Morrish was the longest serving "custodian" of Fudge's Firewater until he retired in 1998. The business and the Firewater were then acquired by the Lifestyle Pharmacy Group, who managed them until 2001 when the East Street Pharmacy was acquired by Moss Chemists Ltd; Mr David Conroy was its manager until 2005, and he continued to make and supply Fudge's Firewater.

Gee's linctus itself gradually fell out of favour as a cough medicine because of the problem of abuse. Finding commercial sources of the linctus became more difficult, and temporary interruptions to the availability of Fudge's Firewater occurred early in the twenty-first century. Then, in January 2006, a notice appeared on the window of Bridport's East Street Pharmacy (owned by Moss/Alliance) announcing that the medicine would be discontinued owing to 'problems with the supply of ingredients'. That was the official line, but the author suspects that this was not the full story. Towards the end of 2005, there had been a change in the pharmacy regulations[10] whereby extemporaneously prepared medicines or nostrums containing Schedule 5 controlled drugs became prescription only medicines. Fudge's Firewater, with its small amounts of morphine, was affected by this change. It could no longer be sold over the counter and patients wanting the medicine would need a private prescription. Perhaps Moss/Alliance judged that this would seriously weaken sales and so decided to discontinue the medicine.

That was not quite the end however, because in the same year, Fudge's Firewater began to be sold by Mr Dipan Shah of the St John's Pharmacy in Weymouth, Dorset, about 20 miles south east of Bridport. He continued to make and supply a modified version of the medicine for the next three years. However, the result of the change in pharmacy regulations (see above) meant that people needed to persuade their doctor to issue a private prescription if they wanted it.

Not surprisingly the need for a private prescription, and the cost entailed, severely affected sales, and coupled with increasingly stringent regulations for mixing medicines in pharmacies, production finally ceased in 2009. For all these reasons, Fudge's Firewater is very unlikely ever to reappear.

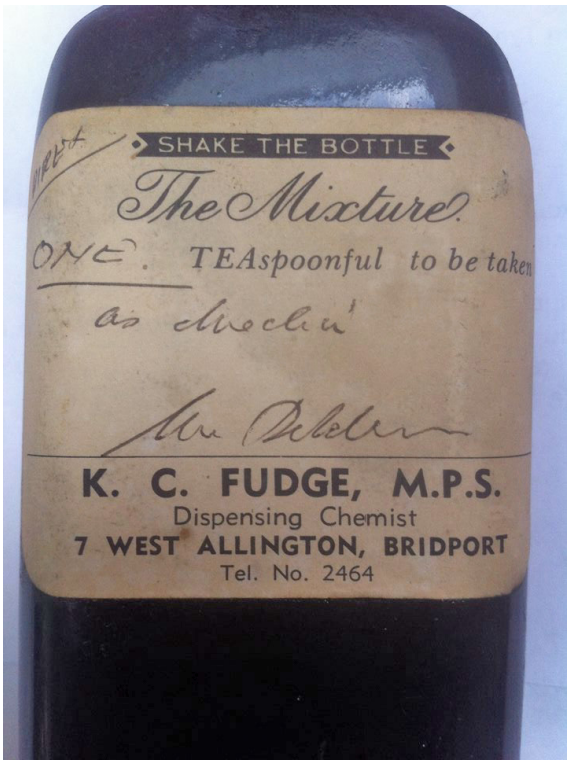

Figure 3. *One of Mr Fudge's bottles (probably about 50 years old) (Source: Photo kindly supplied by Jamie Dibdin)*

Conclusion

Fudge's Firewater served Bridport well for 50 years. Although the medicine is now just a memory it is an important part of Bridport's history and one deserving of being preserved. It also has an important place in the history of British pharmacy. At the very time Fudge's Firewater was introduced many nostrums were beginning to disappear, following the introduction of the National Health Service in 1948, the expansion of proprietary medicines in the post-war period, and the growth of advertising in both magazines and on television.

Fudge's Firewater is a rare example of a nostrum that survived into the twenty-first century. Furthermore, ownership of the recipe changed hands several times, the pharmacy where it was made and sold also changed hands on a number of occasions, and the product continued even when the home pharmacy was in corporate ownership. Although in the end the recipe moved to a pharmacy in a different town, the demise of Fudge's Firewater was the result of changes in pharmacy regulations.

Chemist's nostrums are however still very much with us. The current regulations are published by the General Pharmaceutical Council in their *Guidance for Registered Pharmacies Preparing Unlicensed Medicines* (May 2014). This states that 'an unlicensed medicine that is prepared with the intention of selling it over the counter (one that is not a prescription-only medicine) is often called a 'Chemist's Nostrum.'[11]

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SHORT COMMUNICATION

Cataloguing nature's 'library': The doctrine of signatures in Western thought and practice

Owen Durant

Abstract

Generally viewed as a quaint, if puzzling, relic of the folk medical tradition, the Doctrine of Signatures and wider concepts of 'sympathetic magic' have informed selection patterns of natural medicines the world over. Associations between form and perceived medical value are idiosyncratic and culture specific. Briefly considered here are the factors that led to the development of a Doctrine of Signatures in the western tradition and what lessons it might impart when re-considered as an evolving series of ideas, rather than as a single doctrine.

Introduction

Faced with a multitude of unfamiliar and often dangerous plants that potentially held the keys to life and death, our ancestors needed ways to map and distinguish the helpful and harmful from the merely ineffectual. One such way was to ascribe meaning to an object's shape, colour, location, smell or taste–seeking 'clues' from these characteristics to indicate likely medicinal purpose.

For example, a plant resembling a lung (e.g. *Pulmonaria officinalis* L.) could be used to treat respiratory illness; red coloured plants (e.g. *Vinca rosea* L.) might be used to cure blood conditions; plants found near a river (e.g. *Salix alba* L.) could be beneficial in the treatment of water-borne diseases. At the same time, sweet smelling (e.g. *Acorus* spp.) or bitter tasting plants (e.g. *Momordica charantia* L.) could be used to combat diseases attributed to excessive bitterness (e.g. Kidney or Spleen disorders) or excessive sweetness (e.g. Diabetes).

By finding similarities, patterns or *signatures* would emerge which could guide foragers and be passed into collective knowledge. Some even believed that plants spoke to them in hallucenogenic rituals (e.g. *Ayahuasca*) conveying secrets of their curative powers.

Even animal parts and fossils were believed to possess healing properties that could be inferred from their outward appearance. Traditions as diverse as the Scandinavian and the Native American record the use of Elk's hoof as a remedy for 'falling sickness' (epilepsy) based on the Elk's behavior of using its hoof to relieve itself from 'vertigo'; the kidney shaped Jew's Stone (*Lapis judaicus)* which appears in Discorides' *De Materia Medica* became a widely accepted cure for kidney stones. Over time, such 'sympathetic magic' would develop into recognizable medical systems such as *Ayurveda* and *Unani* and, in Western belief, into a 'Doctrine' of Signatures.

Cataloguing Nature's 'Library'

The earliest humans most probably derived information about plants from observing animals. Their proximity to and total reliance on their surroundings for nourishment and medicine made it important that they could recognize signs of sickness and cure.

Zoopharmacognosy, the branch of science that seeks to understand animals' self-medication, particularly in the primate kingdom, has identified 'strong similarities' in plant selection criteria between humans and chimpanzees.[1]

Notable is the shared use of rough leaves of certain *Ficus* species for the alleviation of pain associated with intestinal parasites.

Selection criteria such as leaf texture, smell and taste have no doubt contributed to recognition of medicinal attributes and are, in certain ways, easier to identify than perceived physical resemblance to an organ.[2] However, these qualities are still subject to a wide spectrum of interpretation.

How can perceptual and often esoteric impressions be objectively assessed? The answer may be, simply, that they cannot be studied bio-scientifically.[3] Calling the Doctrine of Signatures 'largely untestable' Bennett, nevertheless, attempted a meta-analysis of botanical nomenclature, looking at the descriptive suffix *cordata* (heart) to investigate whether this suffix corresponded to instances of reported cardiac therapeutic use. Using a sample of some 80 plant binomials he found there to be no significant correlation. However, the attempt to link what are known to be subjective descriptions to medicinal use can only paint a partial picture at best. Bennett concluded, among other things, that signatures acted as a mnemonic (memory aiding) device and should be regarded as '*post hoc* attributions rather than *a priori* clues' to plant use.

I would suggest, with the necessity for communication over generations, signatures represent something more systematized than mere memory aids. Unable to document their pharmacopoeia, pre-literate societies learned to 'read' plants and these signatures evolved to function as 'catalogue numbers' in a natural 'library'.

How these 'catalogue numbers' were determined and assigned would, of course, vary - according to time, place and culture. For example, *Pulmonaria officinalis* L., (lungwort), present in the northern United States, popular in Europe as a respiratory medicine and astringent, has no recorded medicinal use in North America.

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In contrast, *Scutellaria lateriflora L.,* (skullcap), a native of North America, known to be anti-convulsive and sedative in the European pharmacopeia has no equivalent Native American medicinal use.[4, 5]

Religion and Reformation

The 'Doctrine' of Signatures itself is, according to the American Anthropologist Daniel E. Moerman, a 'European' idea. Porter (2006) believes that the Doctrine of Signatures 'evolved gradually over the centuries'.[6] Dyer (1889) wrote that the Doctrine of Signatures was 'a development of the much older notion of a real connection between object and image'.[7] Duffin (2008) states that the Doctrine of Signatures' roots are 'firmly based on Aristotelian principles'.[8]

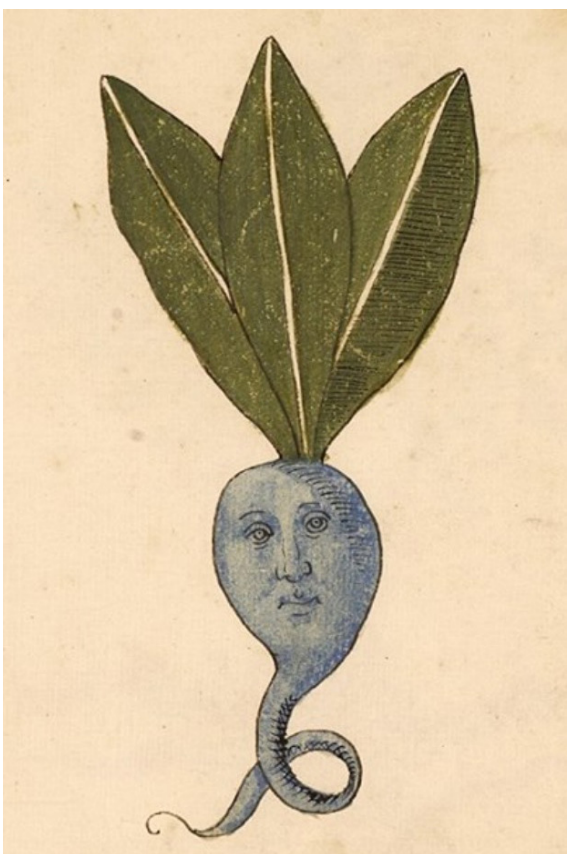

Figure 1. *Illustration of mandrake from a fifteenth century Northern Italian herbal (author unknown)*
(Source: Schoenberg Institute for Manuscript Studies at University of Pennsylvania Libraries)

In many respects the Doctrine of Signatures fits more comfortably into the realm of religion rather than science. Some of the earliest recorded references to the Doctrine of Signatures are found in the Old Testament (Genesis 30:14-16) where the anthropomorphic mandrake (Figure 1) appears as an aphrodisiac and cure for impotence. The concept re-surfaces in Franciscan Friar Albertus Magnus' *De Mineralibus* (c. 1260) and the first natural history encyclopedia, *Hortus Sanitatis* (1484).

In the febrile climate of Reformation-era Europe, the Doctrine of Signatures remained something in which Christians could still agree. The writings of religious mystics, such as Jakob Böhme (1575-1624) concerning cosmic signatures, would foreshadow the 'new age' worldview with its emphasis on the intrinsic unity of nature. Although the term signature implicitly suggests an author and Creator, Böhme's ideas, in particular, are closer to the Eastern ones of Hinduism and Buddhism with their concepts of *prana* and *qi* - a 'life force' permeating everyone and everything.

Figure 2. *Plants of the Asteracae family; one of multiple plates in della Porta's Phytognomica (1588)*
(Source: The Wellcome Library)

In 1588 the Italian polymath Giambattista della Porta (1535-1615) published the influential *Phytognomonica* which bridged the gulf between animism and rationalism. With its systematically juxtaposed images of body and plant parts (Figure 2) *Phytognomonica* displays evidence of a proto-scientific method.[9] Indeed, for della Porta, true Natural Magick (as opposed to sorcery), was 'nothing else but the survey of the whole course of nature'.[10]

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A Curious Paradox

At its core, the Doctrine of Signatures presents a profound conundrum. Hippocrates (460-370 BC) codified the prevailing medical opinion of his time with the observation: *similia similibus curentur* (by similar things are the sick made healthy); yet, a parallel, but seemingly diametrically opposed, notion of *contraria contrariis remedium* (opposites cure opposites) found its expression in the later Galenic model. Both incorporated remedies based on a Doctrine of Signatures-like rationale and this led to the formation of two distinct branches of homeopathic and antipathic medical practice.

So, how do we reconcile these two linked but apparently contradictory practices? I would argue that clues can be found in the much earlier Vedic concept of *nirdvandva* (cf. Carl Jung) or the transcending of opposites; the 'oneness' of creation rendering distinctions and, therefore, opposites obsolete.[11]

Such 'harmonic' thinking, as reflected in the *yin* and *yang* of Chinese Taoism, was ultimately displaced in the West by dualism, which sought to construct discrete opposing categories of things and ideas. *Similia similibus curentur* nevertheless survived as the foundation for Samuel Hahnemman's (1755-1843) Law of Similars, which underpins modern Homeopathy.[12]

A Doctrine in Decline

Over time, the Doctrine of Signatures became unable to hold the multiplicity of ideas within it. As early as the sixteenth century Dodoens (1517-1585), the famed Flemish Physician and Herbalist, branded the Doctrine of Signatures 'so changeable and uncertain that it seems absolutely unworthy of acceptance'. Berdoe (1836-1916), writing in 1888-whilst elsewhere lauding Paracelsus (1493-1541) as the 'Luther' of medicine and chemical science, labelled his Doctrine of Signatures as 'very curious and most absurd'.[13] By the twentieth century 'faith' in the Doctrine of Signatures had become the marginal preserve of homeopaths, herbalists and spiritualists.

To its detriment, herbalism at its most reactionary has continued to promote the Doctrine of Signatures unquestioningly even when demonstrably harmful. For example, *Aristolochia clematitis* L. (birthwort) - selected for its supposed resemblance to the womb and birth canal and used historically for the treatment of women in childbirth - has in recent years been found to contain highly nephrotoxic and oncogenic aristolochic acid.[14]

Conclusion

Despite Western medicine's rejection of the Doctrine of Signatures as animistic; superstitious; magical or even dangerous echoes of it persist in tradition-based medical systems (*e.g.* Traditional Chinese Medicine or TCM) which are of growing popular interest in the West and are, increasingly, the focus of serious ethnopharmacological studies which demonstrate the integrity of traditional healing categories and the superior reliability of ethnopharmacologically based drug leads. [15,16,17]

In the same way that attempts to justify the Doctrine of Signatures have been labelled as examples of *post hoc* attribution, our evaluation - of a doctrine - rather than of the disparate ideas which it contains could be seen in a similar light; a fundamental misunderstanding clouded by history.

Perhaps, it is now time we stopped viewing the Doctrine of Signatures as a doctrine at all, but rather a series of interwoven, but distinct, ethnomedical concepts which, given a more sympathetic interpretation, could pass the insight of previous generations into our hands. Stripped of dogma, the Doctrine of Signatures speaks a proto-scientific truth–that a closer reading of our natural 'literature' might lead us to a more dynamic and fruitful relationship with the content of nature's 'library'.

Acknowledgements

Thanks are due to Professor Michael Heinrich, Peter G. Homan and Professor Daniel E. Moerman.

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150 years on: Joseph Lister and 'The Antiseptic Principle in the Practice of Surgery'

Ursula Lang

Abstract
It is 150 years since Joseph Lister published his seminal paper entitled 'On the Antiseptic Principle in the Practice of Surgery.' This short communication summarizes the background to this paper, and concludes that Lister fully deserves the title 'father of modern antisepsis.'

Zusammenfassung
Vor 150 Jahren publizierte Joseph Lister seinen wegweisenden Aufsatz zur Anwendung antiseptischer Verfahren in der Chirurgie. Diese kurze Darstellung fasst die Beweggründe zusammen, die Lister zu seiner Publikation veranlassten und folgert daraus, dass Lister den Titel 'Vater der modernen Antispesis' völlig zurecht verdient.

Lister's paper in the *British Medical Journal*

On 21 September 1867 the British surgeon Joseph Lister (1827-1912) published a paper entitled 'On the Antiseptic Principle in the Practice of Surgery' in the *British Medical Journal*.[1] It rapidly attracted the attention of numerous physicians.[2] He introduced his ground-breaking essay with the following words:

> 'In the course of an extended investigation into the nature of inflammation, and the healthy and morbid conditions of the blood in relation to it, I arrived several years ago at the conclusion that the essential cause of suppuration in wounds is decomposition, brought about by influence of the atmosphere upon blood or serum retained within them, and, in the case of contused wounds, upon portions of tissue destroyed by the violence of the injury'.

Lister was influenced by the researches of the French chemist Louis Pasteur (1822-1895) who had demonstrated that putrefaction was not caused by oxygen or any gases, but by minute vital organisms suspended in the air.[3] He was persuaded that *'materials capable of destroying the life of the floating particles could avoid decomposition in the injured parts'*. He expounded the use of carbolic acid as an antiseptic substance of great effectiveness:

> 'The material which I have employed is carbolic or phenic acid, a volatile organic compound which appears to exercise a peculiarly destructive influence upon low forms of life, and hence is the most powerful antiseptic with which we are at present acquainted.'

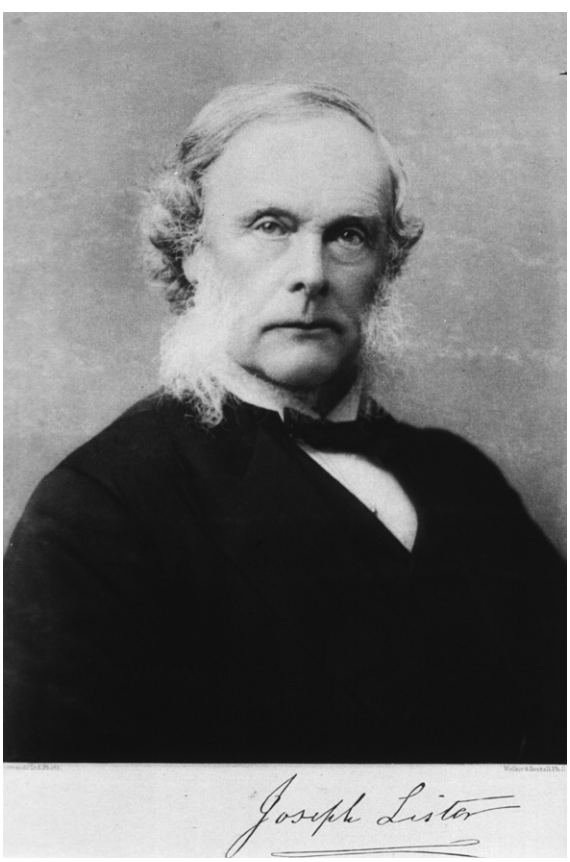

Figure 1. *Joseph Lister (1827-1912)*

Use of carbolic acid

Lister used carbolic acid in cases of compound fractures that formerly had often resulted in inflammation and eventually amputations:

> 'In conducting the treatment, the first object must be the destruction of any septic germs which may have been introduced into the wound, either at the moment of the accident or during the time which has since elapsed'.

He advocated *'the application of a piece of lint dipped in the acid, overlapping the sound skin to some extent and covered with a tin cap, which was daily raised in order to touch the surface of the lint with the antiseptic.'* This procedure should, he declared, prevent the entrance of septic germs into the wound. The antiseptic treatment had to be continued '*during the first few days after the accident, when the acid originally applied has been washed out or dissipated by absorption and evaporation'*.

Lister referenced his publications in the *Lancet* in March and April 1867, and specified an improved pro-

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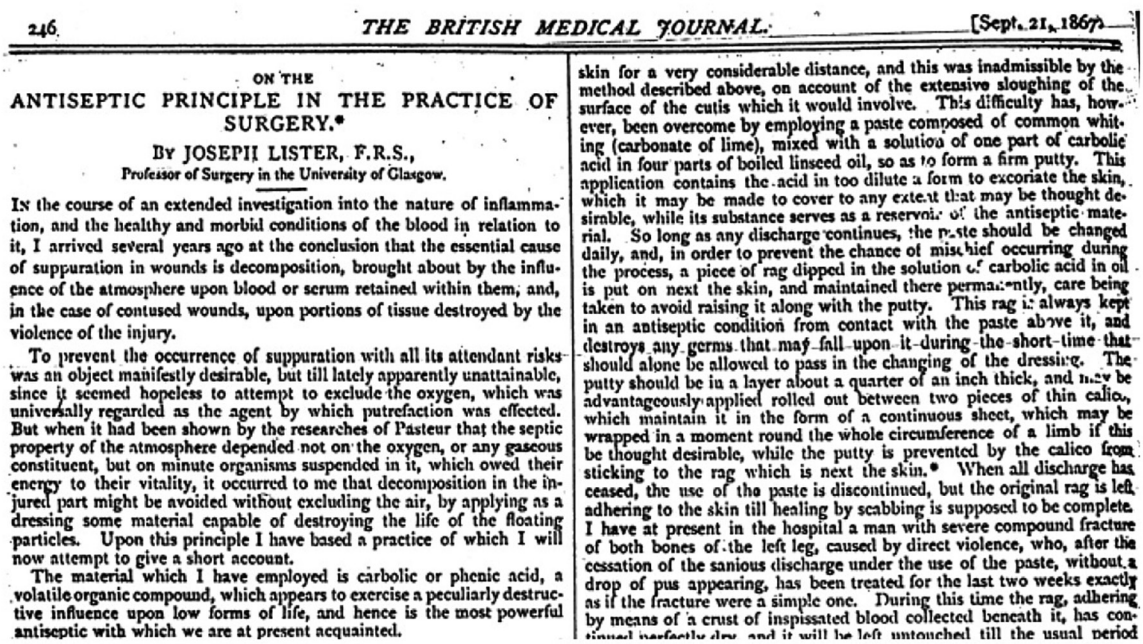
cedure by using antiseptic paste composed of carbonate of lime, mixed with a solution of carbolic acid in boiled linseed oil. Accordingly, the firm putty served as a reservoir for the carbolic acid which was diluted thereby and was less irritating to the skin. Lister noted that carbolic acid itself could induce inflammatory suppuration of the surface of the skin by a process of chemical stimulation. However, on the contrary, 'decomposing substances' were 'self-propagating and self-aggravating poisons' that spread from the surface into recesses and blood'.

> tions, my wards […] have completely changed their character; so that during the last nine months not a single instance of pyaemia, hospital gangrene or erysipelas has occurred in them. As there appears to be no doubt regarding the cause of this change, the importance of the fact can hardly be exaggerated.'

In the following years many antiseptic substances with less toxicity and better compatibility were tested by innumerable surgeons. But the honour of the title



246. THE BRITISH MEDICAL JOURNAL. [Sept. 21, 1867.

ON THE

ANTISEPTIC PRINCIPLE IN THE PRACTICE OF SURGERY.*

By JOSEPH LISTER, F.R.S.,

Professor of Surgery in the University of Glasgow.

In the course of an extended investigation into the nature of inflammation, and the healthy and morbid conditions of the blood in relation to it, I arrived several years ago at the conclusion that the essential cause of suppuration in wounds is decomposition, brought about by the influence of the atmosphere upon blood or serum retained within them, and, in the case of contused wounds, upon portions of tissue destroyed by the violence of the injury.

To prevent the occurrence of suppuration with all its attendant risks was an object manifestly desirable, but till lately apparently unattainable, since it seemed hopeless to attempt to exclude the oxygen, which was universally regarded as the agent by which putrefaction was effected. But when it had been shown by the researches of Pasteur that the septic property of the atmosphere depended not on the oxygen, or any gaseous constituent, but on minute organisms suspended in it, which owed their energy to their vitality, it occurred to me that decomposition in the injured part might be avoided without excluding the air, by applying as a dressing some material capable of destroying the life of the floating particles. Upon this principle I have based a practice of which I will now attempt to give a short account.

The material which I have employed is carbolic or phenic acid, a volatile organic compound, which appears to exercise a peculiarly destructive influence upon low forms of life, and hence is the most powerful antiseptic with which we are at present acquainted.

skin for a very considerable distance, and this was inadmissible by the method described above, on account of the extensive sloughing of the surface of the cutis which it would involve. This difficulty has, however, been overcome by employing a paste composed of common whiting (carbonate of lime), mixed with a solution of one part of carbolic acid in four parts of boiled linseed oil, so as to form a firm putty. This application contains the acid in too dilute a form to excoriate the skin, which it may be made to cover to any extent that may be thought desirable, while its substance serves as a reservoir of the antiseptic material. So long as any discharge continues, the paste should be changed daily, and, in order to prevent the chance of mischief occurring during the process, a piece of rag dipped in the solution of carbolic acid in oil is put on next the skin, and maintained there permanently, care being taken to avoid raising it along with the putty. This rag is always kept in an antiseptic condition from contact with the paste above it, and destroys any germs that may fall upon it during the short time that should alone be allowed to pass in the changing of the dressing. The putty should be in a layer about a quarter of an inch thick, and may be advantageously applied rolled out between two pieces of thin calico, which maintain it in the form of a continuous sheet, which may be wrapped in a moment round the whole circumference of a limb if this be thought desirable, while the putty is prevented by the calico from sticking to the rag which is next the skin.* When all discharge has ceased, the use of the paste is discontinued, but the original rag is left adhering to the skin till healing by scabbing is supposed to be complete. I have at present in the hospital a man with severe compound fracture of both bones of the left leg, caused by direct violence, who, after the cessation of the sanious discharge under the use of the paste, without a drop of pus appearing, has been treated for the last two weeks exactly as if the fracture were a simple one. During this time the rag, adhering by means of a crust of inspissated blood collected beneath it, has continued perfectly dry, and it will be left untouched till the usual period

Figure 2. *Part of first page of 'on the Antiseptic Principle in the Practice of Surgery,' 1867*

Lister furthermore described the successful antiseptic treatment of abscesses, contused and lacerated wounds and recommended improved methods of applying ligatures. Additionally, during the performance of an operation, a solution of carbolic acid in twenty parts of water should destroy '*any septic germs that may fall upon the wound*'.

Conclusion

Lister finished his essay with a remarkable and self-confident statement:

> 'But since the antiseptic treatment has been brought into full operation, and wounds and abscesses no longer poison the atmosphere with putrid exhala-

'father of modern antisepsis,' the man who saved thousands of lives, is rightly due to Joseph Lister.

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BOOK REVIEW

Van gildekast tot schoenendoos: Nederlandse simpliciaverzamelingen

By Raymond van der Ham and Annette Bierman

Leiden, The Netherlands: Erato, 2017. Pp 156. Paperback, price €20.00 including postage. ISBN 978-94-92165-17-6. Available from order@stichtingfarmaceutischerfgoed.nl. This book is the fifth in the series *Venster op farmaciehistorie* published on behalf of the Kring voor de Geschiedenis van de Pharmacie in Benelux (Cercle Benelux d'Histoire de la Pharmacie).

Reviewed by Christopher J. Duffin

One gets the impression that materia medica or 'simplicia' cabinets (i.e. collections of medicinal simples) are rare survivals of pharmaceutical material culture. This book, whose title could be rendered in English as 'From guild cabinet to shoe box: Dutch simplicia Collections' indicates that, at least in the Netherlands, they are well represented, and the authors present an extremely useful survey of surviving collections.

In the Introduction, the authors explain how collections of simples were necessary for the members of pharmacy guilds, their assistants, and later on the examining bodies that tested and certificated their knowledge; they were also prized by individual doctors, surgeons and midwives. While the pharmacopoeia was in a state of flux, such collections acted as reference material until the recommendations of the national pharmacopoeia had stabilised. They also helped the medical professional to distinguish between authentic and fraudulent medical ingredients.

From an analysis of simplicia cabinets as advertised in various types of sales literature – advertisements, auction catalogues, etc. – from the 17th century onwards, the authors discovered that descriptions tended to focus on the quality of the box itself, the type of wood from which it was constructed, and the number of trays and cells for holding the medicinal simples themselves. They also found, perhaps unsurprisingly, that the cabinets were most commonly owned by doctors, pharmacists, surgeons and master midwives, although they were also found in the collections (*naturalienkabinet*) of a range of non-medical personnel. These latter examples might often contain non-pharmaceutical objects of naturalia – geological, zoological and herbal specimens. Various College and institutional inventories give an indication as to the subsequent loss of many cabinets. Indeed, the authors conclude that the survivals (probably around 4%) represent only the 'tip of the iceberg' in comparison to the number of cabinets that were once in circulation.

Johannes Brosterhuysen (1596-1650), a student at Leiden, wrote to Constantine Huygens (1608-1687), giving advice as to what simples should be included in a materia medica cabinet, based upon his own collection. Slightly later (1662) a simplicia cabinet was delivered to the Pharmaceutical College in the Hague; it remained in use until the second half of the nineteenth century.

The heyday of simplicia cabinet production seems to have been during the eighteenth and nineteenth centuries, with literally hundreds being offered for sale in the Netherlands. The design and architecture of the cabinet itself were extremely diverse with the number of trays ranging from 6 to 100. Contents do not seem to have been standardised; most simples were kept unpackaged in their requisite trays, but later cabinets might include vials or glass slides. From 1890 onwards, the component simples were increasingly stored in sealed glass tubes and other containers supplied by the industry, rather than open trays. This meant that elaborate storage cabinets became progressively less necessary and represented an un-necessary expense; materials packaged in specially designed Bakelite, plastic or glass

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containers could be stored in a box on the shelf – hence the reference to 'shoe box' in the title of the book.

The authors conclude that, while older materia medica cabinets are known from England and elsewhere, the possession of a simplicia cabinet by an individual for anything other than teaching is somewhat unique to the Netherlands, and something of an expression of the Dutch obsession, from the seventeenth century onwards, for collecting material culture.

The bulk of the volume consists of a descriptive catalogue of 54 surviving simplicia cabinets, the oldest dated to 1660, classified according to packaging materials: A, open or sealed boxes; B, sealed glass tubes, bottles or jars; C, paper sachets with transparent windows, pots or plastic tubes and boxes; D, glass pots, bottles and the like; E, others. Each cabinet is fully described with details of its current location, size, date of production, owner (if known), and history with occasional comments on the contents. Most entries are presented as a double page spread with good quality colour illustrations of both the cabinet itself, and representatives of the associated drawers and their contents. Also, the text is supported with a comprehensive bibliography. The book is nicely printed on high quality glossy paper in A4 format.

Publications on materia medica cabinets are very sparse and – clearly a labour of love by the authors – this volume provides a welcome survey of Dutch survivals. Worth the cover price for the illustrations alone, this book fills a gap in the literature, and will be of particular interest to those interested in the history of pharmacy and the development of the materia medica.

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